

**CLAIMS**

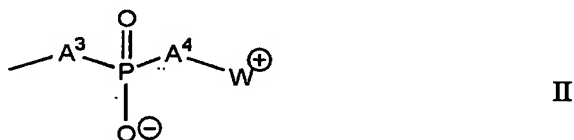
1. A therapeutic or diagnostic composition comprising particles of a polymer matrix into which is absorbed aqueous liquid, the particles having diameters in the range 40 to 4000  $\mu\text{m}$ , characterised in that surfaces of the particles express zwitterionic groups.

2. A composition according to claim 1 in which the polymer matrix is substantially non-biodegradable.

3. A composition according to claim 1 or claim 2 which comprises a continuous aqueous medium in an amount sufficient to suspend the particles.

4. A composition according to any preceding claim which is sterile.

5. A composition according to any preceding claim in which the zwitterionic group is ammonium, phosphonium, or sulphonium phosphate or phosphonate ester zwitterionic group, more preferably a group of the general formula II



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in which the moieties  $\text{A}^3$  and  $\text{A}^4$ , which are the same or different, are -O-, -S-, -NH- or a valence bond, preferably -O-, and  $\text{W}^+$  is a group comprising an ammonium, phosphonium or sulphonium cationic group and a group linking the anionic and cationic moieties which is preferably a  $\text{C}_{1-12}$ -alkanediy l group,

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preferably in which  $\text{W}^+$  is a group of formula  $-\text{W}^1-\text{N}^+\text{R}_3$ ,  $-\text{W}^1-\text{P}^+\text{R}_4$ ,  $-\text{W}^1-\text{S}^+\text{R}_4$  or  $-\text{W}^1-\text{Het}^+$  in which:

$\text{W}^1$  is alkanediy l of 1 or more, preferably 2-6 carbon atoms optionally containing one or more ethylenically unsaturated double or triple bonds, disubstituted-aryl (arylene), alkylene arylene, arylene alkylene, or alkylene aryl alkylene, cycloalkanediy l, alkylene cycloalkyl, cycloalkyl alkylene or

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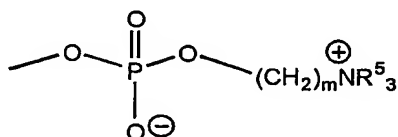
alkylene cycloalkyl alkylene, which group W<sup>1</sup> optionally contains one or more fluorine substituents and/or one or more functional groups; and

either the groups R<sup>3</sup> are the same or different and each is hydrogen or alkyl of 1 to 4 carbon atoms, preferably methyl, or aryl, such as phenyl, or two of the groups R<sup>3</sup> together with the nitrogen atom to which they are attached form an aliphatic heterocyclic ring containing from 5 to 7 atoms, or the three groups R<sup>3</sup> together with the nitrogen atom to which they are attached as heteroaromatic ring having 5 to 7 atoms, either of which rings may be fused with another saturated or unsaturated ring to form a fused ring structure containing from 5 to 7 atoms in each ring, and optionally one or more of the groups R<sup>3</sup> is substituted by a hydrophilic functional group, and

the groups R<sup>4</sup> are the same or different and each is R<sup>3</sup> or a group OR<sup>3</sup>, where R<sup>3</sup> is as defined above; or

Het is an aromatic nitrogen-, phosphorus- or sulphur-, preferably nitrogen-, containing ring, for example pyridine.

6. A composition according to claim 5 in which the zwitterionic group has general formula III



III

where the groups R<sup>5</sup> are the same or different and each is hydrogen or C<sub>1-4</sub> alkyl, and m is from 1 to 4, in which preferably the groups R<sup>5</sup> are the same preferably methyl.

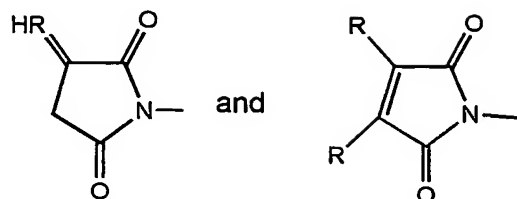
7. A composition according to any preceding claim in which the zwitterionic groups are pendant groups on a polymer formed from ethylenically unsaturated monomers including a monomer of the general formula I



in which Y is an ethylenically unsaturated group selected from H<sub>2</sub>C=CR-CO-A-, H<sub>2</sub>C=CR-C<sub>6</sub>H<sub>4</sub>-A<sup>1</sup>-, H<sub>2</sub>C=CR-CH<sub>2</sub>-A<sup>2</sup>-, R<sup>2</sup>O-CO-CR=CR-CO-O-, RCH=CH-



5



A is -O- or  $\text{NR}^1$ ;

$\text{A}^1$  is selected from a bond,  $(\text{CH}_2)_l\text{A}^2$  and  $(\text{CH}_2)_l\text{SO}_3^-$  in which  $l$  is 1 to 12;

10  $\text{A}^2$  is selected from a bond, -O-, O-CO-, CO-O, CO- $\text{NR}^1$ -, - $\text{NR}^1$ -CO, O-CO- $\text{NR}^1$ -,  $\text{NR}^1$ -CO-O-;

R is hydrogen or  $\text{C}_{1-4}$  alkyl;

$\text{R}^1$  is hydrogen,  $\text{C}_{1-4}$  alkyl or  $\text{BX}$ ;

$\text{R}^2$  is hydrogen or  $\text{C}_{1-4}$  alkyl;

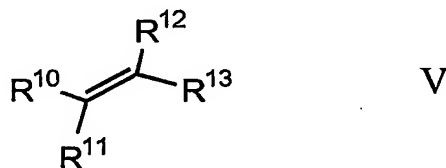
15 B is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxaalkylene) group, optionally containing one or more fluorine substituents;

X is the zwitterionic group.

8. A composition according to claim 7 in which Y is  $\text{H}_2\text{C}=\text{CR}-\text{CO}-$   
20 A, preferably in which R is hydrogen or methyl and preferably in which A is O or NH.

9. A composition according to claim 7 or claim 8 in which the ethylenically unsaturated monomers further comprise comonomers, for instance compounds of the general formula V

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in which  $\text{R}^{10}$  is selected from hydrogen, halogen,  $\text{C}_{1-4}$  alkyl and groups  
30  $\text{COOR}^{14}$  in which  $\text{R}^{14}$  is selected from hydrogen and  $\text{C}_{1-4}$  alkyl;

$\text{R}^{11}$  is selected from hydrogen, halogen and  $\text{C}_{1-4}$  alkyl;

$R^{12}$  is selected from hydrogen, halogen,  $C_{1-4}$  alkyl and groups  $COOR^{14}$  provided that  $R^{10}$  and  $R^{12}$  are not both  $COOR^{14}$ ; and

$R^{13}$  is a  $C_{1-10}$  alkyl, a  $C_{1-20}$  alkoxy carbonyl, a mono- or di- ( $C_{1-20}$  alkyl) amino carbonyl, a  $C_{6-20}$  aryl (including alkaryl) a  $C_{7-20}$  aralkyl, a  $C_{6-20}$  aryloxy carbonyl, a  $C_{1-20}$  -aralkyloxy carbonyl, a  $C_{6-20}$  arylamino carbonyl, a  $C_{7-20}$  aralkyl-amino, a hydroxyl or a  $C_{2-10}$  acyloxy group, any of which may have one or more substituents selected from halogen atoms, alkoxy, oligo-alkoxy, aryloxy, acyloxy, acylamino, amine (including mono and di-alkyl amino and trialkylammonium in which the alkyl groups may be substituted), carboxyl, sulphonyl, phosphoryl, phosphino, (including mono- and di- alkyl phosphine and tri-alkylphosphonium), zwitterionic, hydroxyl groups, vinyloxy carbonyl and other vinylic or allylic substituents, and reactive silyl or silyloxy groups, such as trialkoxysilyl groups;

or  $R^{13}$  and  $R^{12}$  or  $R^{13}$  and  $R^{11}$  may together form  $-CONR^{15}CO$  in which  $R^{15}$  is a  $C_{1-20}$  alkyl group.

10. A composition according to claim 9 in which the comonomer is a non-ionic comonomer, such as a  $C_{1-24}$  alkyl(alk)-acrylate or -acrylamide, mono- or di- hydroxy- $C_{1-6}$ -alkyl(alk)-acrylate, or -acrylamide, oligo( $C_{2-3}$  alkoxy)  $C_{2-18}$ -alkyl (alk)-acrylate, or -acrylamide, acrylamide styrene, vinylacetate or N-vinyl lactam.

11. A composition according to any preceding claim in which the matrix polymer is a polyion complex.

12. A composition according to any of claims 1 to 10 in which the polymer matrix is covalently crosslinked.

13. A composition according to claim 12 in which the matrix polymer is formed from ethylenically unsaturated monomers including a di- or higher-valent ethylenically unsaturated monomer.

14. A composition according to claim 12 in which covalent crosslinking has been carried out by reaction of functional groups on preformed polymer subjected to conditions whereby intermolecular reaction takes place to form covalent bonds.

15. A composition according to any preceding claim in which the matrix polymer is based on polyvinylalcohol.

16. A composition according to claim 15 in which the polyvinyl alcohol is crosslinked by reaction of pendant ethylenically unsaturated crosslinking groups by radical polymerisation.

17. A composition according to any preceding claim in which the particles, when imbibed with physiological saline at room have a water content of at least 30% by weight, preferably at least 50% by weight.

18. A composition according to any preceding claim in which the particles are substantially spherical.

19. A composition according to any preceding claim, in which the diameters of the particles, when fully imbibed with water, are in the range 150  $\mu\text{m}$  to 3000  $\mu\text{m}$ , preferably in the range 200 to 2000  $\mu\text{m}$ .

20. A composition according to any preceding claim which is stable on storage at room temperature such that the particles do not coalesce to the extent that they cannot be redispersed upon gentle agitation.

21. Use of polymer particles in the manufacture of a composition according to any preceding claim for administration to an animal for therapy or diagnosis.

22. Use according to claim 21 in which the composition is administered to form an embolous.

23. Use according to claim 22 in which the composition is administered for uterine fibroid embolisation, embolisation of vessels around tumours or tumour-excision sites, embolisation of varicose veins or varicoceles, embolisation of arteriovenous malformations or venous malformations, hemostasis of gastro-intestinal bleeds, embolisation of fistulas or embolisation of fallopian tubes, or seminiferous tubes for sterilisation purposes.

24. Microspheres comprising a core which is a matrix of a water-insoluble water-absorbing polymer, which when imbibed with physiological saline at equilibrium at room temperature have diameters in the range 40 to

4000  $\mu\text{m}$ , characterised by expressing zwitterions over their external surfaces.

25. Microspheres according to claim 24, which when fully imbibed with physiological saline have a water content of at least 30% by weight, preferably at least 50% by weight.

26. A composition according to claim 24 or claim 25 having the features defined in any of the claims 2 to 17.

27. A kit comprising, each in separate vessels, a plurality of populations of microspheres according to claim 24 or 25, the populations differing in respect of the range of particle diameters.

28. A kit according to claim 27 in which the size range of each of the populations of microspheres, when imbibed with physiological saline to equilibrium at room temperature, is 50 to 1000  $\mu\text{m}$ , preferably 150 to 300  $\mu\text{m}$ .

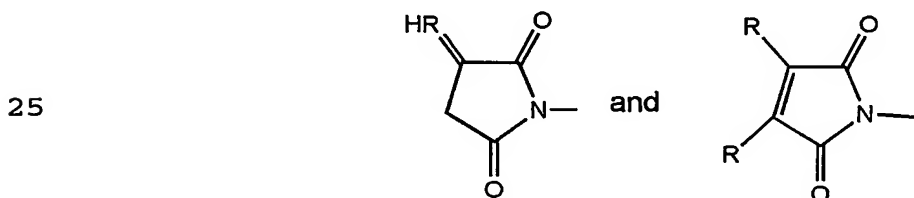
29. A kit according to claim 28 in which the diameters of the different populations substantially do not overlap with one another.

30. A process of inverse suspension polymerisation in which ethylenically unsaturated monomers including a zwitterionic monomer of the general formula I

Y B X

I

in which Y is an ethylenically unsaturated group selected from  $\text{H}_2\text{C}=\text{CR}-\text{CO}-\text{A}-$ ,  $\text{H}_2\text{C}=\text{CR}-\text{C}_6\text{H}_4-\text{A}^1-$ ,  $\text{H}_2\text{C}=\text{CR}-\text{CH}_2\text{A}^2$ ,  $\text{R}^2\text{O}-\text{CO}-\text{CR}=\text{CR}-\text{CO}-\text{O}$ ,  $\text{RCH}=\text{CH}-\text{CO}-\text{O}$ ,  $\text{RCH}=\text{C}(\text{COOR}^2)\text{CH}_2-\text{CO}-\text{O}$ ,



A is  $-\text{O}-$  or  $\text{NR}^1$ ;

$\text{A}^1$  is selected from a bond,  $(\text{CH}_2)_l\text{A}^2$  and  $(\text{CH}_2)_l\text{SO}_3^-$  in which l is 1 to 12;

$\text{A}^2$  is selected from a bond,  $-\text{O}-$ ,  $\text{O}-\text{CO}-$ ,  $\text{CO}-\text{O}$ ,  $\text{CO}-\text{NR}^1-$ ,  $-\text{NR}^1-\text{CO}$ ,  $\text{O}-$

CO-NR<sup>1</sup>-, NR<sup>1</sup>-CO-O-;

R is hydrogen or C<sub>1-4</sub> alkyl;

R<sup>1</sup> is hydrogen, C<sub>1-4</sub> alkyl or BX;

R<sup>2</sup> is hydrogen or C<sub>1-4</sub> alkyl;

5 B is a bond, or a straight branched alkanediyl, alkylene oxaalkylene, or alkylene (oligooxalkylene) group, optionally containing one or more fluorine substituents;

X is the zwitterionic group and miscible comonomers, as a liquid monomer mixture, are dispersed into a continuous liquid non-solvent to form  
10 a dispersed phase, and initiator is added to initiate radical polymerisation in the dispersed phase, and the particles of polymer formed from the dispersed phase are recovered.

31. A process according to claim 30 in which the ethylenically unsaturated monomers include di- or higher functional crosslinking monomer.

15 32. A process according to claim 30 or claim 31 in which the monomer mixture comprises water.

33. A process according to any of claims 30, 31, or 32 in which the non solvent comprises a water-in-oil stabiliser prior to addition of the monomer mixture.